

Remarks

Reconsideration of this Application is respectfully requested.

Claims 49-57 and 59-68 are pending in the application, with claim 49 being the sole independent claim. Although no claim amendments have been made, the pending claims are presented for the Examiner's convenience.

Based on the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding rejections and that they be withdrawn.

Claim Rejections under 35 U.S.C. Section 103(a)

Claims 49-55, 57, 59-61, 63, 66 and 68 were rejected as being unpatentable over Lachenmeier et al. (*Biotechniques* 13:124-131, 1992) and Pruitt (*Gene* 66:121-134, 1988) and further in view of Rubenstein et al. (*Nucl. Acids. Res.* 18:4833-4842, 1990). Applicants respectfully note that the first author of the Lachenmeier reference is G. Fry, thus this reference should be referred to as Fry *et al.* The Office Action states that:

the ordinary skilled artisan seeking to develop a method for recovering ssDNA molecules from a mixture of such molecules, would have been motivated to combine the teachings of Lachenmeier et al. of recovering ssDNA using hybridization to a haptenylated probe and ligand-conjugated matrix, with the teachings of Pruitt and Rubenstein et al., teaching routine techniques of using optimum hybridization conditions, as well as using plasmid or phagemid cloning comprising a library of target sequences. Furthermore, it would have been a routine matter to convert ssDNA into dsDNA prior to transformation with the added benefit of increased transformation efficiency, due to increased structural stability inherent in dsDNA as compared to ssDNA.

See Office Action, p. 4-5. Applicants respectfully traverse. Establishing *prima facie* obviousness requires a showing that each claim element is taught or suggested by the prior art. See *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). Specifically, establishing *prima facie* obviousness requires a showing that some combination of objective teachings in the art and / or knowledge available to one of skill in the art would have lead that individual to arrive at the claimed invention. See *In re Fine*, 5 USPQ2d 1596, 1598 (Fed. Cir. 1988). Moreover, establishing *prima facie* obviousness requires not only that such a combination of prior art teachings is possible, but also that the teachings would have (a) motivated the skilled artisan to make the combination to arrive at the claimed invention, and (b) suggested to the skilled artisan a reasonable likelihood of success in making and using the claimed invention. See *In re Dow Chem. Co.*, 837 F.2d 469, 473 (Fed. Cir. 1988). Absent a showing of such motivation and suggestion, *prima facie* obviousness is not established. See *In re Fine*, 5 USPQ2d at 1598.

The Court of Appeals for the Federal Circuit specifically instructed in *Tec-Air, Inc. v. Dense Manufacturing Michigan Inc.*, 192 F.3d 1353 (Fed. Cir. 1999), that

There is no suggestion to combine... if a reference teaches away from its combination with another source.' ... A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant . . . [or] if it suggests that the line of development flowing from the reference's disclosure is unlikely to be productive of the result sought by the applicant.' *In re Gurley* . . . (Fed. Cir. 1994).

The Court of Appeals for the Federal Circuit further instructed that "references that teach away cannot serve to create a *prima facie* case of obviousness" (*In re Gurley*, 27 F.3d

551, 553 (Fed. Cir. 1994)), and that an “applicant may rebut a *prima facie* case of obviousness by showing that the prior art teaches away from the claimed invention in any material respect” (*In re Geisler*, 116 F.3d 1465, 1469 (Fed. Cir. 1997)).

A *prima facie* case of obviousness of claims 49-55, 57, 59-61, 63, 66 and 68 over Fry *et al.* and Pruitt and further in view of Rubenstein *et al.* has not been established. Nothing in these references would have motivated the skilled artisan to combine them to arrive at the claimed invention. If anything, the cited references teach away from the claimed invention. As was the case in *Tec-Air*, the skilled artisan reading the cited references “would be led in a direction divergent from the path that was taken by the applicant.”

Claims 49-55, 57, 59-61, 63, 66 and 68 are directed to recovering circular single-stranded DNA molecules using haptenylated nucleic acid probes bound to a support, releasing the haptenylated probes, and converting the circular ssDNA molecules into dsDNA molecules.

Fry *et al.* disclose a ***sequencing*** method in which a sequence of interest within an M13 phage vector is obtained by hybridization to a biotinylated synthetic oligonucleotide probe coupled to a streptavidin-coated paramagnetic particle. The ***single-stranded DNA molecule*** obtained by this procedure is then used directly as a DNA sequencing template. A double-stranded molecule is not formed in the sequencing method of Fry *et al.* The Office Action states that it would have been a routine matter to convert ssDNA into dsDNA prior to transformation due to increased stability of dsDNA compared to ssDNA as taught by the secondary references, Pruitt and Rubenstein *et al.* Applicants respectfully note that while it may in fact be a routine matter to convert ssDNA into dsDNA, a skilled artisan reading and

aiming to practice the sequencing method of Fry *et al.* would never do such a thing. This is because the sequencing methods taught by Fry *et al.* would no longer work for their intended purpose, namely sequencing of a single-stranded DNA molecule. The methods disclosed by the secondary references would result in a double-stranded DNA molecule that would not be suitable for use as a single-stranded DNA template for sequencing according to the methods taught by Fry *et al.* The reason that Fry *et al.* do not teach the conversion of the recovered single stranded molecules to double-stranded molecules is that the disclosed sequencing method would not work. Those skilled in the art would recognize this, and certainly would not be motivated to employ the single- to double-stranded DNA conversion methods of Pruitt and Rubenstein *et al.* to practice the sequencing method of Fry *et al.* If anything, the skilled artisan would be discouraged from combining the sequencing method taught by Fry *et al.* with the methods of Pruitt and Rubenstein *et al.*

Because nothing in these references would have motivated the skilled artisan to combine these references to arrive at the claimed invention, a *prima facie* showing of obviousness cannot be properly be maintained. Applicants therefore respectfully request that the Examiner reconsider and withdraw the rejection under 35 U.S.C. §103(a).

The remaining rejections under 35 U.S.C. § 103(a) (items 2-4 in the Office Action at pages 5-8) are also based on the Fry *et al.* reference, and involve other secondary references (Rigas *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* 83:9591-9595, 1986; Symons, U.S. Patent No. 4,898,951; and Knappe *et al.* (U.S. Patent No. 5,989,867). These secondary references are cited against various dependent claims. The pending claims recite that one or more circular single-stranded nucleic acid molecules are converted to double stranded nucleic acid

molecules. The primary and secondary references, alone or in combination, fail to teach this conversion step. Because a claim element is absent from these references, there is no motivation to combine them to arrive at the claimed invention and a *prima facie* case of obviousness cannot be established.

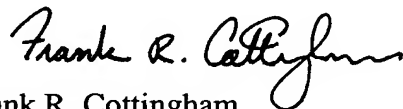
Applicants therefore respectfully request that the Examiner reconsider and withdraw the rejections under 35 U.S.C. §103(a).

Conclusion

All of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided. Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.



Frank R. Cottingham
Attorney for Applicants
Registration No. 50,437

Date: JAN. 19, 2005

1100 New York Avenue, N.W.
Washington, D.C. 20005-3934
(202) 371-2600